

TENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents
United States Patent and Trademark
Office
Box PCT
Washington, D.C.20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 04 October 2000 (04.10.00)	
International application No. PCT/US00/00942	Applicant's or agent's file reference 249/167
International filing date (day/month/year) 14 January 2000 (14.01.00)	Priority date (day/month/year) 14 January 1999 (14.01.99)
Applicant YOUNG, Andrew et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

08 August 2000 (08.08.00)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Pascal Piriou

Telephone No.: (41-22) 338.83.38

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 249/167	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/US 00/ 00942	International filing date (day/month/year) 14/01/2000	(Earliest) Priority Date (day/month/year) 14/01/1999
Applicant AMYLIN PHARMACEUTICALS, INC.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☒ furnished subsequently to this Authority in written form.

☒ furnished subsequently to this Authority in computer readable form.

☒ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☒ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of Invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No

P S 00/00942

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K38/22 A61K47/48 A61P5/48 A61P17/00 A61P35/00
//C07K14/575

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, STRAND, WPI Data, PAJ, BIOSIS, MEDLINE, CANCERLIT, CHEM ABS Data, EMBASE, SCISEARCH

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 46584 A (GOEKE BURKHARD JOHANNES ;HOFFMANN EIKE (DE); GOEKE RUEDIGER (DE);) 11 December 1997 (1997-12-11)	1,4-6
Y	page 1, line 1 -page 3, line 22 page 10, line 14 -page 11, line 11 ---	2,3,7,8
Y	PASSA P ET AL: "MECHANISMS SUPPRESSING GLUCAGON SECRETIONS IN GLUCAGONOMAS" DIABETOLOGIA, vol. 19, no. 3, 1980, page 305 XP000938466 ISSN: 0012-186X the whole document --- -/--	2,3

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- "&" document member of the same patent family

Date of the actual completion of the international search

18 August 2000

Date of mailing of the international search report

01/09/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Stein, A

INTERNATIONAL SEARCH REPORT

International Application No

P S 00/00942

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	FRANCIS GE ET AL: "PEGylation of cytokines and other therapeutic proteins and peptides: the importance of biological optimisation of coupling techniques" INTERNATIONAL JOURNAL OF HEMATOLOGY, vol. 68, no. 1, July 1998 (1998-07), pages 1-18, XP000938448 cited in the application the whole document	7,8
A	US 5 424 286 A (ENG JOHN) 13 June 1995 (1995-06-13) cited in the application the whole document	1-8
A	WO 98 05351 A (YOUNG ANDREW A ;AMYLIN PHARMACEUTICALS INC (US); BEELEY NIGEL ROBE) 12 February 1998 (1998-02-12) especially page 27 line 3 - line 9 the whole document	1,4-8

INTERNATIONAL SEARCH REPORT

on patent family members

International Application No

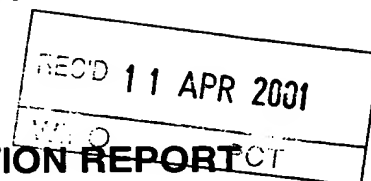
P S 00/00942

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
W0 9746584	A	11-12-1997	DE 19622502 A DE 19637230 A AU 3173297 A BR 9710452 A CN 1227567 A EP 0915910 A	02-01-1998 19-03-1998 05-01-1998 17-08-1999 01-09-1999 19-05-1999
US 5424286	A	13-06-1995	NONE	
W0 9805351	A	12-02-1998	AU 4063697 A EP 0966297 A	25-02-1998 29-12-1999

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)



Applicant's or agent's file reference N.80234	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US00/00942	International filing date (day/month/year) 14/01/2000	Priority date (day/month/year) 14/01/1999
International Patent Classification (IPC) or national classification and IPC A61K38/00		
Applicant AMYLIN PHARMACEUTICALS, INC. et al.		



- This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
- This REPORT consists of a total of 7 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

 These annexes consist of a total of sheets.

- This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 08/08/2000	Date of completion of this report 05.04.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Perez, F Telephone No. +49 89 2399 7338 

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/00942

I. Basis of this report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1-67 as originally filed

Claims, No.:

1-8 as originally filed

Drawings, sheets:

1/26-26/26 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US00/00942

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 1-8 (IA).

because:

☒ the said international application, or the said claims Nos. 1-8 (industrial applicability) relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N) Yes: Claims 2-3, 7-8

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US00/00942

	No:	Claims	1, 4-6
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-8
Industrial applicability (IA)	Yes:	Claims	1-8 see separate sheet
	No:	Claims	

2. Citations and explanations
see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US00/00942

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. **Claims 1-8** relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34.4(a)(i) PCT).

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

2. Reference is made to the following documents:

D1: WO 97 46584 A (GOEKE BURKHARD JOHANNES ;HOFFMANN EIKE (DE); GOEKE RUEDIGER (DE);) 11 December 1997.

D2: PASSA P ET AL. DIABETOLOGIA, vol. 19, no. 3, 1980, page 305.

D3: FRANCIS GE ET AL. INTERNATIONAL JOURNAL OF HEMATOLOGY, vol. 68, no. 1, July 1998 (1998-07), pages 1-18.

D4: US-A-5 424 286 (ENG JOHN) 13 June 1995 (1995-06-13).

D5: WO 98 05351 A (YOUNG ANDREW A ;AMYLIN PHARMACEUTICALS INC (US); BEELEY NIGEL ROBE) 12 February 1998.

3. Novelty (Articles 33.1 and 33.2 PCT)

D1 discloses that exendin analog, and particularly exendin-3 and exendin-4 inhibit the liberation of glucagon in human (page 10 line 14 - page 11 line 11). Therefore, **claims 1, 4-6** lack novelty.

Claims 2-3 and 7-8 are restricted to specific conditions or to the use of specific compounds which are not disclosed in the prior art. Hence **claims 2-3, 7-8** are novel.

4. Inventive Step (Articles 33.1 and 33.3 PCT)

The present application relate to methods for lowering glucagon level using exendin or

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US00/00942

analogs, in particular to treat necrolytic migratory erythema and glucagonoma.

D2 which is considered to be the closest prior art suggests to treat glucogonomas and necrolytic migratory erythema using somatostatin to reduce glucagon synthesis.

The technical problem to be solved by the present application is therefore to find alternative compounds to treat glucogonomas and necrolytic migratory erythema by reducing glucagon level.

The solution proposed in the present application consist in using exendin or exendin analogs.

D1 discloses that exendin has the property of reducing glucagon secretion. It would be obvious to the person skilled in the art, namely when the same result is to be achieved (reducing glucagon level), to use exendin analog with corresponding effect to the use of somatostatin according to document D2, thereby arriving to the solution proposed in this application. Moreover the use of PEGylated compounds does not seems to bring any unexpected advantage as D3 discloses the advantages of PEGylation of therapeutics peptides.

The subject-matter of **claims 1-8** does therefore not involve an inventive step (Article 33(3) PCT).

5. Industrial applicability (Articles 33.1 and 33.4 PCT)

For the assessment of the present **claims 1-8** on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re It m VII

C rtain d fects in the int rnational application

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US00/00942

6. Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D1 and D2 is not mentioned in the description, nor are these documents identified therein.

09889.331

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(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
20 July 2000 (20.07.2000)

PCT

(10) International Publication Number
WO 00/41548 A3

(51) International Patent Classification⁷: **A61K 38/22**,
47/48, A61P 5/48, 17/00, 35/00 // C07K 14/575

(74) Agent: **DUFT, Bradford, J.**; Lyon & Lyon LLP, 633 West
Fifth Street, Suite 4700, Los Angeles, CA 90071-2066
(US).

(21) International Application Number: PCT/US00/00942

(81) Designated States (*national*): AE, AL, AM, AT, AU, AZ,
BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK,
DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,
IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,
LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT,
RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA,
UG, US, UZ, VN, YU, ZA, ZW.

(22) International Filing Date: 14 January 2000 (14.01.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/116,380 14 January 1999 (14.01.1999) US
60/132,017 30 April 1999 (30.04.1999) US
60/175,365 10 January 2000 (10.01.2000) US

(84) Designated States (*regional*): ARIPO patent (GH, GM,
KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent
(AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent
(AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU,
MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM,
GA, GN, GW, ML, MR, NE, SN, TD, TG).

(71) Applicant (*for all designated States except US*): **AMYLIN
PHARMACEUTICALS, INC.** [US/US]; 9373 Towne
Centre Drive, Suite 250, San Diego, CA 92121 (US).

Published:
— with international search report

(72) Inventors; and
(75) Inventors/Applicants (*for US only*): **YOUNG, Andrew**
[US/US]; P. O. Box 60591, Point Loma, CA 92166 (US).
GEDULIN, Bronislava [US/US]; 12825 Stebick Court,
San Diego, CA 92131 (US).

(88) Date of publication of the international search report:
29 November 2001

*For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*



WO 00/41548 A3

(54) Title: METHODS FOR GLUCAGON SUPPRESSION

(57) Abstract: Methods for use of an exendin, an exendin agonist, or a modified exendin or exendin agonist having an exendin or exendin agonist linked to one or more polyethylene glycol polymers, for example, for lowering glucagon levels and/or suppressing glucagon secretion in a subject are provided. These methods are useful in treating hyperglucagonemia and other conditions that would be benefited by lowering plasma glucagon or suppressing glucagon secretion.

INTERNATIONAL SEARCH REPORT

Int. Application No

PCT/US 00/00942

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K38/22 A61K47/48 A61P5/48 A61P17/00 A61P35/00
//C07K14/575

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, STRAND, WPI Data, PAJ, BIOSIS, MEDLINE, CANCERLIT, CHEM ABS Data, EMBASE, SCISEARCH

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 46584 A (GOEKE BURKHARD JOHANNES ;HOFFMANN EIKE (DE); GOEKE RUEDIGER (DE);) 11 December 1997 (1997-12-11)	1,4-6
Y	page 1, line 1 -page 3, line 22 page 10, line 14 -page 11, line 11	2,3,7,8
Y	PASSA P ET AL: "MECHANISMS SUPPRESSING GLUCAGON SECRETIONS IN GLUCAGONOMAS" DIABETOLOGIA, vol. 19, no. 3, 1980, page 305 XP000938466 ISSN: 0012-186X the whole document	2,3

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

18 August 2000

Date of mailing of the international search report

01/09/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
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Authorized officer

Stein, A

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/00942

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	FRANCIS GE ET AL: "PEGylation of cytokines and other therapeutic proteins and peptides: the importance of biological optimisation of coupling techniques" INTERNATIONAL JOURNAL OF HEMATOLOGY, vol. 68, no. 1, July 1998 (1998-07), pages 1-18, XP000938448 cited in the application the whole document	7,8
A	US 5 424 286 A (ENG JOHN) 13 June 1995 (1995-06-13) cited in the application the whole document	1-8
A	WO 98 05351 A (YOUNG ANDREW A ; AMYLIN PHARMACEUTICALS INC (US); BEELEY NIGEL ROBE) 12 February 1998 (1998-02-12) especially page 27 line 3 - line 9 the whole document	1,4-8

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 00/00942

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 1-8 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/00942

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9746584 A	11-12-1997	DE 19622502 A DE 19637230 A AU 3173297 A BR 9710452 A CN 1227567 A EP 0915910 A	02-01-1998 19-03-1998 05-01-1998 17-08-1999 01-09-1999 19-05-1999
US 5424286 A	13-06-1995	NONE	
WO 9805351 A	12-02-1998	AU 4063697 A EP 0966297 A	25-02-1998 29-12-1999